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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,987	DICKSON ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-33* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 1-33 are pending in the application and are currently under prosecution.

2. It is noted that claim 18 has not been restricted as drawn to cancer invasion or metastasis because there is no antecedent basis for the term "condition" as drawn to malignancies in claim 16 from which claim 18 depends. If Applicant were to amend the claims to provide proper antecedent basis, claim 18 as drawn to cancer invasion or metastasis will be restricted.

3. In the interests of compact prosecution, it is noted that the claims are replete with misspellings, for example "pecific" in claim 12 and "weherein" in claims 24 and 31, "epiethlium" in claim 19. Given these misspellings in the claims, it is suggested that Applicant review the specification for these informalities because both the claims and the specification will be objected to upon examination of the elected invention and correction will be required

4. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

3. It is noted that the claims of the instant application have been determined to include linking claims. Claim 1 links Groups 1-9. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional

statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1. Claims 1-7 and claim 15 (as it is drawn to cells of a premalignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a pre-malignant lesion comprising assaying for activated matriptase, classified in Class 435, subclass 7.1.

Group 2. Claims 1-7 and claim 15 (as it is drawn to cells of a malignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a malignant lesion comprising assaying for activated matriptase, classified in Class 435, subclass 7.1.

Group 3. Claims 1-7 and claim 15 (as it is drawn to cells of a pathology other than a pre-malignant or malignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a pathology other than a pre-malignant or malignant lesion comprising assaying for activated matriptase, classified in Class 435, subclass 7.1.

Group 4. Claims 1-2, 8-13 and claim 15 (as it is drawn to cells of a premalignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a pre-malignant lesion comprising assaying for activated matriptase further comprising exposing the sample to one or more antibodies which do not specifically bind to activated matriptase, classified in Class 435, subclass 7.1.

Group 5. Claims 1-7 and claim 15 (as it is drawn to cells of a malignant lesion) are drawn to an *in vitro* method of diagnosing the presence

of a malignant lesion comprising assaying for activated matriptase further comprising exposing the sample to one or more antibodies which do not specifically bind to activated matriptase, classified in Class 435, subclass 7.1.

Group 6. Claims 1-7 and claim 15 (and claim 15 (as it is drawn to cells of a pathology other than a pre-malignant or malignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a pathology other than a pre-malignant or malignant lesion comprising assaying for activated matriptase further comprising exposing the sample to one or more antibodies which do not specifically bind to activated matriptase, classified in Class 435, subclass 7.1.

Group 7. Claims 1, 14 are drawn to an *in vitro* method of diagnosing the presence of a pre-malignant lesion comprising assaying for activated matriptase further comprising detecting the presence an/or measuring the concentration in the sample of matriptase cognate inhibitor HA1-1 (M58), classified in Class 435, subclass 7.1.

Group 8. Claims 1, 14 and claim 15 (as it is drawn to cells of a malignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a malignant lesion comprising assaying for activated matriptase further comprising detecting the presence an/or measuring the concentration in the sample of matriptase cognate inhibitor HA1-1 (M58), classified in Class 435, subclass 7.1.

Group 9. Claims 1, 14 and claim 15 (as it is drawn to cells of a pathology other than a pre-malignant or malignant lesion) are drawn to an *in vitro* method of diagnosing the presence of a pathology other than a pre-

malignant or malignant lesion comprising assaying for activated matriptase further comprising detecting the presence an/or measuring the concentration in the sample of matriptase cognate inhibitor HA1-1 (M58), classified in Class 435, subclass 7.1.

4. It is noted that the claims of the instant application have been determined to include linking claims. Claim 16, as it is drawn to malignancies, links Groups 10-13. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), 16. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 10. Claims 16, 17, 20-22 are drawn to a method of treating malignancies characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which directly blocks the activity of active matriptase in an epithelial tissue, classified in Class 424, subclass 130.1.

Group 11. Claims 16, 17, 20-22 are drawn to a method of treating malignancies characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which directly blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase, classified in Class 424, subclass 130.1.

Group 12. Claims 16, 17, 22-26 are drawn to a method of treating malignancies characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in an epithelial tissue by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

Group 13. Claims 16, 17, 22-26 are drawn to a method of treating malignancies characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

5. It is noted that the claims of the instant application have been determined to include linking claims. Claim 16, as it is drawn to premalignant conditions links Groups 14-17/(a)-(c)/(I)-(XI). The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), 16. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application.

Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 14. Claims 16-22 are drawn to a method of treating pre-malignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which directly blocks the activity of active matriptase in an epithelial tissue, classified in Class 424, subclass 130.1.

Group 15. Claims 16-22 are drawn to a method of treating premalignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

Group 16. Claims 16-19, 22-26 are drawn to a method of treating pre-malignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in an epithelial tissue by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

Group 17. Claims 16-19, 22-26 are drawn to a method of treating premalignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

For each of the inventions 14-17 above, restriction to one of the following is also required under 35 USC121. Therefore, election is required of one of inventions 14-17 and one of inventions (a)-(c). It is noted that this is not an election of species requirement in that each of the linked groups consists of one of inventions 14-17 above and one of inventions (a)-(c) below.

(a) tissue remodeling

(b) inflammatory responses

© smooth muscle proliferation

For each of the inventions 14-17 and (a)-(c) above, restriction to one of the following is also required under 35 USC121. Therefore, election is required of one of inventions 14-17 and one of inventions (a)-(c) and one of inventions (I)-(vI). It is noted that this is not an election of species requirement in that each of the linked groups consists of one of inventions 14-17 and one of inventions (a)-(c) above and one of inventions (I)-(Ivii) below.

(I) atypical ductal hyperplasia of the breast

(II) actinic keratosis (AK)

(III) leukoplakia

(IV) Barrett's epithelium (columnar metaplasia) of the esophagus

(V) Ulcerative colitis

(VI) Adenomatous colorectal polyps

(VII) Erythroplasia of Queyrat

(VIII) Bowen's disease

(IX) Bowenoid papulosis

(X) Vulvar intraepithelial neoplasia (VIN

(XI) Displatic changes to the cervix

6. It is noted that the claims of the instant application have been determined to include linking claims. Claim 16, as it is drawn to pathologic conditions other than malignancies or pre-malignant conditions links Groups 18-21/(a)-(c). The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), 16. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 18. Claims 16-18, 20-22 are drawn to a method of treating pathologic conditions other than malignancies and premalignant conditions

characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which directly blocks the activity of active matriptase in an epithelial tissue, classified in Class 424, subclass 130.1.

Group 19. Claims 16-18, 22 are drawn to a method of treating pathologic conditions other than malignancies and premalignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

Group 20. Claims 16-19, 22-26 are drawn to a method of treating pathologic conditions other than malignancies and premalignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in an epithelial tissue by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

Group 21. Claims 16-19, 22-26 are drawn to a method of treating pathologic conditions other than malignancies and premalignant conditions characterized by the activated form of matriptase comprising administering a therapeutically effective amount of an agent which blocks the activity of active matriptase in a tissue other than an epithelial tissue which expresses matriptase by blocking the activity of an agent capable of inducing the activation of matriptase, classified in Class 514, subclass 2+.

For each of the inventions 18-21 above, restriction to one of the following is also required under 35 USC121. Therefore, election is required of one of inventions 18-21 and one of inventions (a)-(c). It is noted that this is not an election of species requirement in that each of the linked groups consists of one of inventions 18-21 above and one of inventions (a)-(c) below.

(a) tissue remodeling

(b) inflammatory responses

© smooth muscle proliferation

7. It is noted that the claims of the instant application have been determined to include linking claims. Claim 27, as it is drawn to pathologic conditions other than malignancies or pre-malignant conditions links Groups 22-23. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), 27. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 22. Claims 27-30 are drawn to a method of treating pathologic conditions characterized by the lack of the activated form of matriptase

comprising administering a therapeutically effective amount of an agent capable of inducing activation of matriptase wherein said agent comprises serum, Classified in Class 514, subclass 2+.

Group 23. Claims 27-28, 31-33 are drawn to a method of treating pathologic conditions characterized by the lack of the activated form of matriptase comprising administering a therapeutically effective amount of an agent capable of inducing activation of matriptase wherein said agent is a lipoprotein, Classified in Class 514, subclass 2+.

8. The inventions are distinct, each from the other because of the following reasons:

Inventions 1-13, 14-17/(a)-(c)/(I)-(XI), 18-21/(a)-(c), 22-23 are materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success.

9. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or recognized divergent subject matter, restriction for examination purposes as indicated is proper.

10. Groups 1-6, 10-11, 14-15, 18-19 are further subject to election of a single disclosed species.

Claims 1, 16 are generic to a plurality of disclosed patentably distinct species comprising antibodies that bind activated matriptase with different structures and functions wherein the antibodies are (a) M69, (b) M123, recited in claims 4, 11, 21.

11. Groups 12-13, 16-17, 20-21, 23 are further subject to election of a single disclosed species.

Claims 16, 27 are generic to a plurality of disclosed patentably distinct species comprising agents capable of inducing activation of matriptase with different structures and functions wherein the agents are (a) LPA, (b) S1P recited in claims 26, 33.

12. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

13. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

15. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 308-0787. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Susan Ungar
Primary Patent Examiner
October 11, 2004